

reporter molecule that is appended to the signaling aptamer prior to binding the ligand comprising the steps of:

appending the reporter molecule to an aptamer via covalent coupling to form the signaling aptamer, wherein the reporter molecule replaces a nucleic acid residue in the aptamer or is inserted between two nucleic acid residues in the aptamer such that the placement does not interfere with the ligand-binding site of the aptamer;

placing the signaling aptamer in solution wherein the signaling aptamer is neither immobilized on a support nor linked to a support;

contacting the signaling aptamer free in solution with the ligand under conditions whereby the signaling aptamer binds the ligand; and

detecting the increase in fluorescence intensity or in colorimetric intensity generated by the reporter molecule transduced by the conformational change in the signaling aptamer upon binding the ligand.

Please amend claim 6 as follows:

6. (amended) The method of claim 1, wherein the covalent coupling of the reporter molecule to the aptamer occurs during chemical synthesis, during transcription or post-transcriptionally.

Please amend claim 7 as follows:

7. (amended) The method of claim 1, wherein the reporter molecule is a dye.

Please amend claim 15 as follows:

15. (twice-amended) A method of transducing the conformational change of a signaling aptamer that occurs upon the signaling aptamer binding a ligand to a detectable increase in fluorescence intensity or in colorimetric intensity generated by a fluorescent dye that is appended to the signaling aptamer prior to binding the ligand comprising the steps:

appending the fluorescent dye to an aptamer via covalent coupling to form the signaling aptamer, wherein the fluorescent dye replaces a nucleic acid residue in the aptamer or is inserted between two nucleic acid residues in the aptamer such that

the placement does not interfere with the ligand-binding site of the aptamer;

placing the signaling aptamer in solution wherein the signaling aptamer is neither immobilized on a support nor linked to a support;

contacting the signaling aptamer in solution with the ligand under conditions whereby the signaling aptamer binds the ligand; and

detecting the increase in fluorescence intensity or in colorimetric intensity generated by the fluorescent dye transduced by the conformational change in the signaling aptamer upon binding the ligand.

Please amend claim 28 to read as follows:

28. (twice-amended) The method of claim 15, wherein the ligand is quantitated by the step comprising:

correlating the increase in fluorescence intensity or in colorimetric intensity generated upon the signaling aptamer binding the ligand with the quantity of ligand bound to the signaling aptamer.

Please cancel claims 2, 5 and 17-18.